

(a) [contacting] bringing into contact a first substance which includes a peptide fragment of p21, or a derivative or analog thereof, comprising an amino acid sequence [molecule which comprises an amino acid sequence] selected from the group consisting of:

RERWNFDFVTETPLEGDFAW (peptide 4) (SEQ ID NO:4);

KACRRFLGPDVDSQLSRDCD (peptide 2) (SEQ ID NO:2);

KxxRRyFzP (wherein x may be any amino acid, y and z may be hydrophobic, and each of the bold residues may be absent or different); (SEQ ID NO:14)

KRRQTSMTDFYHSKRRLIFS (peptide 10) (SEQ ID NO:10);

KRRQTSATDFYHSKRRLIFS [(peptide 10)] (SEQ ID NO:28);

TSMTDFYHSKRRLIFSKRKP (peptide 11) (SEQ ID NO:11);

KRRLIFSK (SEQ ID NO:23); and

xyLzF (wherein y and z are any amino acid and x is preferably R),

[or a derivative, fragment or analog of said fragment,] with a second substance comprising cyclin D1 and/or Cdk4, or a derivative or analog thereof, and [with] a test compound, under conditions wherein, in the absence of the test compound being an inhibitor of interaction or binding of said first and second substances, said [fragment] first substance and said second substance interact or bind; and

(b) determining interaction or binding between said [fragment] first substance and said second substance.

3. (Amended) The method according to [claim 1 or] claim 2 wherein the fragment, derivative or analog of p21 comprises the amino acid sequence of peptide 4.

4. (Twice Amended) The method according to [claim 1] or claim 2 wherein the fragment, derivative or analog of p21 comprises the amino acid sequence **KxxRRyFzP** (SEQ ID NO:14).

5. The method according to claim 4 wherein the fragment, derivative or analog of p21 comprises the amino acid sequence of peptide 2.

6. (Amended) The method according to [claim 1 or] claim 2 wherein the fragment, derivative or analog of p21 comprises the amino acid sequence xyLzF.

7. The method according to claim 6 wherein the fragment, derivative or analog of p21 comprises the amino acid sequence of peptide 10.

8. (Twice Amended) The method according to claim 6 wherein the fragment, derivative or analog of p21 comprises the amino acid sequence KRRLIFSK (SEQ ID NO:23).

9. The method according to claim 8 wherein the fragment, derivative or analog of p21 comprises the amino acid sequence of peptide 11.

10. (Amended) The method according to [any of claims 1 or] claim 2 further comprising testing the ability of the compound to modulate a p21- mediated effect on Cdk4 activity.

11. A method according to claim 10 wherein RB phosphorylation is tested.

12. A method according to claim [10] 1 or 2 wherein induction of G1 cell-cycle arrest is tested.

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17. (Amended) A method comprising [identifying] obtaining a compound which interferes with interaction or binding between p21 and cyclin D1 and/or Cdk4 and/or modulates a p21-mediated effect on Cdk4 activity in accordance with [any of claims 1 or] claim 2, further comprising formulating the compound into a composition including at least one additional component.

31. (Twice Amended) A method of treating a hyperproliferative disorder in a cell which comprises contacting the cell with or causing the cell to express a substance selected from the group consisting of:

- (i) a fragment of p21, or an active portion or derivative thereof;
- (ii) a peptide fragment including the motif xyLzF, wherein y and z are any amino acid and x derivative of said peptide fragment inhibiting Cdk4;
- (iii) a peptide fragment including the motif **KxxRRyFzP** (SEQ ID NO:14), wherein x is any amino acid, y and z may be hydrophobic, and each of the bold residues may be absent or different; and
- (iv) a functional mimetic of (i), (ii) or (iii) with the property of inhibiting Cdk4; such that a hyperproliferative disorder is treated.

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32. (Twice Amended) The method of claim 31 wherein the substance comprises or consists essentially of a peptide fragment with a sequence which is selected from the group consisting of:

RERWNFDFVTETPLEGDFAW (peptide 4) (SEQ ID NO:4);

KACRRLFGPVDSEQLSRDCD (peptide 2) (SEQ ID NO:2);

KRRQTSMTDFYHSKRRLIFS (peptide 10) (SEQ ID NO:10);

KRRQTSATDFYHSKRRLIFS [(peptide 10)] (SEQ ID NO:28);

TSMTDFYHSKRRLIFSKRKP (peptide 11) (SEQ ID NO:11);

and KRRLIFSK (SEQ ID NO:23),

or a functional mimetic of any of these peptide sequences with the property of inhibiting Cdk4.

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33. (Twice Amended) The method of claim 32 wherein the substance consists essentially of the peptide KRRLIFSK (SEQ ID NO:23) or a functional mimetic thereof which inhibits Cdk4.

34. The method of any of claims 31 to 33 wherein the substance is coupled to a carrier for delivery to cells.

35. (Twice Amended) The method of claim 34 wherein the substance is a peptide and is coupled to a carrier peptide with the sequence RQIKIWFQNRRMKWKK (SEQ ID NO:15).

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36. (Twice Amended) A method of ameliorating a disorder characterized by abnormal cell proliferation comprising contacting a cell with the peptide KRRLIFSK (SEQ ID NO:23), or a functional mimetic thereof with the property of inhibiting Cdk4 such that abnormal cell proliferation is ameliorated.

37. The method according to claim 36, wherein the disorder is a hyperproliferative disorder.

38. (Twice Amended) A method of interfering with interaction between p21 and cyclin D1 and/or Cdk4, comprising contacting p21 and/or Cdk4 with a substance which includes a peptide fragment of p21 or a derivative thereof which is selected from the group consisting of:

RERWNFDFVTETPLEGDFAW (peptide 4) (SEQ ID NO:4);

KACRRLFGPVDSEQLSRDCD (peptide 2) (SEQ ID NO:2);

KxxRRyFzP (wherein x may be any amino acid, y and z may be hydrophobic, and each of the bold residues may be absent or different) (SEQ ID NO:14);

KRRQTSMTDFYHSKRRLIFS (peptide 10) (SEQ ID NO:10);

KRRQTSATDFYHSKRRLIFS [(peptide 10)] (SEQ ID NO:28);

TSMTDFYHSKRRLIFSKRKP (peptide 11) (SEQ ID NO:11);

KRRLIFSK (SEQ ID NO:23); and

xyLzF (wherein y and z are any amino acid and x is preferably R);

or a derivative, fragment, analog or functional mimetic of said fragment.

39. (Twice Amended) A method of modulating a p21-mediated effect on Cdk4 activity, the method including contacting p21 and/or Cdk4 with a substance which comprises a peptide fragment of p21, or a derivative thereof, which is selected from the group consisting of:

RERWNFDFVTETPLEGDFAW (peptide 4) (SEQ ID NO:4);

KACRRLFGPVDSEQLSRDCD (peptide 2) (SEQ ID NO:2);

KxxRRyFzP (wherein x may be any amino acid, y and z may be hydrophobic, and each of the bold residues may be absent or different) (SEQ ID NO:14);

KRRQTSMTDFYHSKRRLIFS (peptide 10) (SEQ ID NO:10);

KRRQTSATDFYHSKRRLIFS [(peptide 10)] (SEQ ID NO:28);

TSMTDFYHSKRRLIFSKRKP (peptide 11) (SEQ ID NO:11);

KRRLIFSK (SEQ ID NO:23); and

xyLzF (wherein y and z are any amino acid and x is preferably R);

or a derivative, fragment, analog or functional mimetic of a said fragment.